

**REMARKS**

Claims 29, 30, 32-39, 41, 44, 46-52, and 59-63 are pending. Claims 44, 48-50, 62, and 63 are allowed. Claims 29, 30, 32-39, 41, 46, and 52 are deemed "allowable if rewritten or amended to overcome the objections. Claims 47, 51, 52 and 59-61 are rejected. Claims 59-61 are deemed "allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2<sup>nd</sup> paragraph, and objection." As suggested by the Examiner in the Office Action, Applicant has amended claims 29, 32 and 59. Applicant has also amended claim 47 consistent with the recommendations of the Examiner in the telephonic interview conducted on April 21, 2010, discussed in greater detail below. No claims have been cancelled or withdrawn in this paper.

Applicant is grateful for the courtesies extended by Examiner Babic during the telephonic interview held on April 21, 2010 with the undersigned representative and Gregory Ahrens (Reg. No. 32,957). During that interview, independent claim 47 was discussed in view of Chinese Patent 1,220,995 to Chen ("Chen"), U.S. Patent No. 5,346,994 to Chomczynski ("Chomczynski"), and Focus (1998) 20(2):36 ("Focus"). Examiner Babic maintained the position that step b) of claim 47 did not specifically require that the pH remain in the range recited in step a). While no agreement was reached as to any specific claim language, the Examiner suggested amending claim 47 to recite that the pH of the mixture containing biological sample from step b) remain in the range recited in step a). As discussed in the interview, Examiner Babic felt that such an amendment would render the claims patentable over the cited art and that no further searching was required because the issue of maintaining the pH had already been searched. Thus, Examiner Babic agreed to enter the amendment after final.

In view thereof, Applicant has amended step b) of claim 47 to recite "sedimenting or filtering the mixture containing biological sample to obtain a purified biological sample substantially

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free of DNA, proteins, and cellular components without the use of a hydrophobic solvent and performing phase separation and wherein the pH of the mixture containing biological sample remains in the range from about pH 3.6 to about pH 5.5." Support for this amendment may be found throughout the specification and at least at paragraphs [0035]-[0044] of the published application.

### **Claim Objections**

The Examiner objected to claims 29, 30, 32-39, 41, 46, 52, and 61 because the phrase "an aqueous phases" utilizes improper English. Applicant amended claim 29 and the claims depending therefrom, claims 30, 32-39, 41, 46, 52, and 61, to recite "an aqueous phase," thereby obviating this objection.

The Examiner also objected to claim 32 as depending from cancelled claim 31. Applicant amended claim 32 to depend from claim 29, thereby obviating this objection.

### **Rejections under 35 U.S.C. § 112 paragraph 2**

The Examiner rejected claims 59-61 under 35 U.S.C. § 112, paragraph 2, as allegedly indefinite. Examiner maintains the position that "higher" is a relative term which renders the claim indefinite. Applicant amended claim 59, the only independent claim at issue in this rejection, to recite, in part, "to selectively precipitate RNA molecules greater than 200 bases from the biological sample." Support for this amendment may be found at least at paragraph [0053] of the published application. Applicant respectfully submits that this rejection is overcome and requests that it be withdrawn.

### **Rejections under 35 U.S.C. § 103(a)**

Examiner rejected claims 47, 51, and 52 under 35 U.S.C. § 103(a) as allegedly unpatentable over Chen in view of Chomczynski and further in view of Focus. As discussed above,

Applicant has amended claim 47, the only independent claim at issue and requests withdrawal of the rejection for at least the reasons set forth below.

The method of claim 47 obtains a "purified biological sample substantially free of DNA, proteins, and cellular components without the use of a hydrophobic solvent and performing phase separation and wherein the pH of the mixture containing biological sample remains in the range from about pH 3.6 to about pH 5.5." *See*, step b) of claim 47. Chen, Chomczynski, and Focus, all describe methods of extracting RNA from a biological sample that utilize a hydrophobic solvent and phase separation and that do not maintain the pH over the claimed range during the extraction process. Since none of the cited references disclose methods that obtain a purified sample without the use of a hydrophobic solvent and phase separation at the presently claimed pH range, Applicant respectfully submits that this claim is in a condition for allowance and requests that the rejection be withdrawn.

With regard to Chen, as the Examiner states, Chen discloses "mixing the sample with a hydrophobic solvent . . ." Office Action, page 5. Specifically, steps 2-4 of Chen's method include adding 0.1 ml of chloroform (a hydrophobic solvent) and isoamyl alcohol mixture solution to the sample, centrifuging the mixture, and removing the "top aqueous phase" from the sample. Chen, page 8. The RNA is then precipitated from the aqueous phase with isopropanol followed by a centrifugation step. Chen also only discloses using a minuscule concentration of buffer that is insufficient to maintain the pH of the sample in the claimed range. Thus, Chen discloses a phase separation step prior to the RNA precipitation step and therefore fails to disclose a method of obtaining a "purified biological sample substantially free of DNA, proteins, and cellular components without the use of a hydrophobic solvent and performing a phase separation and wherein the pH of the mixture containing biological sample remains in the range from about pH 3.6 to about pH 5.5."

Chomczynski fails to remedy these deficiencies because the methods disclosed therein also use a hydrophobic solvent and phase separation to extract RNA. Chomczynski specifically describes methods of differentially isolating RNA, DNA, and protein from a biological sample by first homogenizing the sample in an extraction solution and then conducting a phase separation step by adding a "water-insoluble organic solvent, such as chloroform" to the homogenized sample. This mixture forms an aqueous phase containing RNA, an organic phase containing proteins, and an interphase containing DNA. *See Chomczynski, col. 3, line 54 through col. 4, line 35 and col. 5 lines 5-50.* Thus, Chomczynski clearly describes the addition of hydrophobic organic solvents and clearly describes a method utilizing phase separation. Thus, even if one were motivated to combine Chen with Chomczynski, the combination would fail to disclose or suggest a method that obtains a "purified biological sample substantially free of DNA, proteins, and cellular components without the use of a hydrophobic solvent and performing a phase separation and wherein the pH of the mixture containing biological sample remains in the range from about pH 3.6 to about pH 5.5."

Focus also fails to remedy these deficiencies. As the Examiner acknowledges, Focus suggests centrifuging "before adding chloroform at 12,000 x g at 4 C for 10 min to pellet polysaccharides (also pellets genomic DNA)." Focus, page 36. Focus does not address the issue of maintaining the pH within the presently claimed range. Thus, Focus clearly requires the addition of a hydrophobic solvent, i.e., chloroform, at some point during the method in order to obtain purified RNA. Moreover, while Focus suggests centrifuging a sample to pellet polysaccharides and DNA prior to the addition of chloroform, at the very least, this centrifugation step fails to remove proteins. Focus also fails to appreciate maintaining the pH of the biological over the presently claimed range during this centrifugation step. Thus, even if one were motivated to combine Chen, Chomczynski, and Focus, the combination fails to disclose or suggest a method that obtains a "purified biological

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sample substantially free of DNA, proteins, and cellular components without the use of a hydrophobic solvent and performing a phase separation and wherein the pH of the mixture containing biological sample remains in the range from about pH 3.6 to about pH 5.5."

## **CONCLUSION**

As a result of the remarks given herein, Applicant submits that the rejections of the pending claims have been overcome. Therefore, Applicant respectfully submits that this case is in condition for allowance and requests allowance of the pending claims.

If Examiner believes any detailed language of the claims requires further discussion, Examiner is respectfully asked to telephone the undersigned attorney so that the matter may be promptly resolved. Applicant respectfully requests a one month extension. Applicant has submitted all fees believed due herewith. If any fee is deemed due, consider this as an authorization to charge Deposit Account 23-3000 therefor.

Respectfully submitted,

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